#9

FIG. 1a

970	980	990	1000	1010	1020
AGGTTTACCG	CATTTTGACA	CTAGATGGCA	TCCGTCCCAC	GGGTAGCAGG	TCATGAAGCT
TCCAAATGGC	GTAAAACTGT	GATCTACCGT	AGGCAGGGTG	CCCATCGTCC	AGTACTTCGA
1030	1040	1050	1060	1070	1080
GACCAAGGCA	AGTCCTTTCA	GGGGGAAGAA	AATCAGGAAA	AAAAAAAATT	TTAGAAGCAT
CTGGTTCCGT	TCAGGAAAGT	CCCCCTTCTT	TTAGTCCTTT	TTTTTTTTAA	AATCTTCGTA
1090	1100	1110	1120	1130	1140
TTCAAGAAGC	AAGATGGAAT	ATTTGTACAA	AACAGGTGCT	TTCTCCCCCA	CCATGCGACC
AAGTTCTTCG	TTCTACCTTA	TAAACATGTT	TTGTCCACGA	AAGAGGGGGT	GGTACGCTGG
1150	1160	1170	1180	1190	1200
CGGGAGCTCC	ACTGATATGG	ACAGAATAGC	TTTACAGCTA	CATTCAAAAC	ACACACACAC
GCCCTCGAGG	TGACTATACC	TGTCTTATCG	AAATGTCGAT	GTAAGTTTTG	TGTGTGTGTG
1210	1220	1230	1240	1250	1260
ACACACACAC	ACACACACAC	ACACACACAC	ACACACACAT	GTTTTCTTCC	CTCCCTCCAC
TGTGTGTGTG	TGTGTGTGTG	TGTGTGTGTG	TGTGTGTGTA	CAAAAGAAGG	GAGGGACCTC
1270	1280	1290	1300	1310	1320
TTCCTCCCAT	TCTCTGTGGT	CCCAAAGAGA	TGACCATATT	GACTGTAGAA	ATCACACCAC
AAGGAGGGTA	AGAGACACCA	GGGTTTCTCT	ACTGGTATAA	CTGACATCTT	TAGTGTGGTG
1330	1340	1350	1360	1370	1380
CATAAAAGCC	CATCTGGGAG	CCATTTCCAG	ACTGATCTTT	TTATCATTAA	GGTTTGAATT
GTATTTTCGG	GTAGACCCTC	GGTAAAGGTC	TGACTAGAAA	AATAGTAATT	CCAAACTTAA
1390	1400	1410	1420	1430	1440
CTTGCCACGT	GTGGGTTTTA	AGGTTTTTAG	GGATTTTTAT	CTAGCGGCAC	TCACCTGCTT
GAACGGTGCA	CACCCAAAAT	TCCAAAAATC	CCTAAAAATA	GATCGCCGTG	AGTGGACGAA
1450	1460	1470	1480	1490	1500
CCCTGTGAAT	GTTCAGAATT	CACTGGGCTT	GGTCAGCTAA	TGGAAATGAT	CTATGGTTTG
GGGACACTTA	CAAGTCTTAA	GTGACCCGAA	CCAGTCGATT	ACCTTTACTA	GATACCAAAC
1510	1520	1530	1540	1550	1560
ACTTAAATGT	GAAAGGAAAA	AAAAGAAGGG	GGAAAAGGAG	GGAGGGAGAA	AGAGGGGAAG
TGAATTTACA	CTTTCCTTTT	TTTTCTTCCC	CCTTTTCCTC	CCTCCCTCTT	TCTCCCCTTC
1570	1580	1590	1600	1610	1620
GGAAAACTGC	CTTTTATGCC	TATTGCTACT	CTAACATTTT	GTCTCTCACC	TTCCACTTGG
CCTTTTGACG	GAAAATACGG	ATAACGATGA	GATTGTAAAA	CAGAGAGTGG	AAGGTGAACC
1630	1640	1650	1660	1670	1680
TTCTTCAATG	GAAAGACTGG	ATAGAAAGCT	GGGAGCCAGC	CAGGGATAGG	AGGAGTGTGT
AAGAAGTTAC	CTTTCTGACC	TATCTTTCGA	CCCTCGGTCG	GTCCCTATCC	TCCTCACACA
1690	1700	1710	1720	1730	1740
GTGTGTGTGG	GGGGGGGTGG	GCAGCAAGCA	GAGCCTTAGA	GACAGAGAAG	AGCCTGCTAG
CACACACACC	CCCCCCCACC	CGTCGTTCGT	CTCGGAATCT	CTGTCTCTTC	TCGGACGATC
1750	1760	1770	1780	1790	1800
AGAYCATGAG	CTTYCTTTGA	GACCCCTAGT	GCTAACAGGA	ATAGTTCCTA	ACCAGGTAGC
TCTRGTACTC	GAARGAAACT	CTGGGGATCA	CGATTGTCCT	TATCAAGGAT	TGGTCCATCG
1810	1820	1830	1840	1850	1860
TGTGGTCACG	TGACTCGGCT	GGAAGSCCTG	GCTTTGTCTT	TTTGCTTGCT	GTGCAGCCTT
ACACCAGTGC	ACTGAGCCGA	CCTTCSGGAC	CGAAACAGAA	AAACGAACGA	CACGTCGGAA

FIG. 1b

1870	1880	1890	1900	1910	1920
GAACAAACAC	CCTGGCCTCT	TTGAACCCCA	CTATTTCTCA	GCCCTCAGAT	GAAGAAGTAA
CTTGTTTGTG	GGACCGGAGA	AACTTGGGGT	GATAAAGAGT	CGGGAGTCTA	CTTCTTCATT
1930	1940	1950	1960	1970	1980
TGGTACCTTG	GAGGATACTG	ATGGGTTCAA	GTGAACTAGG	GCAGAGGGTG	GAAGGTTTTG
ACCATGGAAC	CTCCTATGAC	TACCCAAGTT	CACTTGATCC	CGTCTCCCAC	CTTCCAAAAC
1990	2000	2010	2020	2030	2040
TAACCATAAA	CTGAAGTGGG	GTGTTGGTTA	GTAAGTAGCC	ATGAATACCA	TAAAAATATC
ATTGGTATTT	GACTTCACCC	CACAACCAAT	CATTCATCGG	TACTTATGGT	ATTTTTATAG
2050	2060	2070	2080	2090	2100
TGTCAGGTGG	CCAGAGCATC	ACTGTGTTCA	GAACACAACG	GCCCACTCAG	AACACGCGGA
ACAGTCCACC	GGTCTCGTAG	TGACACAAGT	CTTGTGTTGC	CGGGTGAGTC	TTGTGCGCCT
2110	2120	2130	2140	2150	2160
CAATTGAAAG	GCACCAACCT	CCGTGCTTCC	TACCCGTTGT	TTTGTTACCG	TGTAAACGCA
GTTAACTTTC	CGTGGTTGGA	GGCACGAAGG	ATGGGCAACA	AAACAATGGC	ACATTTGCGT
2170	2180	2190	2200	2210	2220
ACTCAACTCT	CGGCACTGAA	CAGGCTTTTG	CTGCAGACCT	GGGGTCTGGA	GGTGTTGTCT
TGAGTTGAGA	GCCGTGACTT	GTCCGAAAAC	GACCTCTGGA	CCCCAGACCT	CCACAACAGA
2230	2240	2250	2260	2270	2280
CTGAGACAGG	AAAACTCATC	TTGTTACTAT	GGCATAGTAG	TAACCACGGA	GCTCTGAGAT
GACTCTGTCC	TTTTGAGTAG	AACAATGATA	CCGTATCATC	ATTGGTGCCT	CCAGACTCTA
2290	2300	2310	2320	2330	2340
AGCCCTGAGC	TGGTGCCGTT	TAGAAAAGTT	TGATGCTTTA	GAAAGAAATC	GTGGCTTAAA
TCGGGACTCG	ACCACGGCAA	ATCTTTTCAA	ACTACGAAAT	CTTTCTTTAG	CACCGAATTT
2350	2360	2370	2380	2390	2400
AGAAGCCTAC	CTGGCATGGG	GGCCCATCCT	CTCCAGCCAT	CCGAATCTCA	ATCTGGTCGT
TCTTCGGATG	GACCCTACCC	CCGGGTAGGA	GAGGTCGGTA	GGCTTAGAGT	TAGACCAGCA
2410	2420	2430	2440	2450	2460
GTGCGTAAGA	ATAGAATCCT	CGGAATGGTA	ACCATGTCTT	GCTTTTTCTT	CTGGGCTTGC
CACGCATTCT	TATCTTAGGA	GCCTTACCAT	TGGTACAGAA	CGAAAAAGAA	GACCCGAACG
2470	2480	2490	2500	2510	2520
TGAGGAAGTC	CCAGGCAGCG	TAGACGTCTT	GGGGGTAGGT	CTGGGAAAAA	TCTCCCAAGA
ACTCCTTCAG	GGTCCCTCGC	ATCTGCAGAA	CCCCCATCCA	GACCCTTTTT	AGAGGGTTCT
2530	2540	2550	2560	2570	2580
TTTTAGGAGG	GGCAGGCGGG	GGATGAGAAA	CTTGGAGATT	CGGTAGATCG	CTGTAGAGCA
AAAATCCTCC	CCGTCCGCCC	CCTACTCTTT	GAACCTCTAA	GCCATCTAGC	GACATCTCGT

Punitive transcriptional start site (5'- end of rat brain 5' - race product).

2590	2600	2610	2620	2630	2640
ACTCAGACAG	TCGGCGGCCT	GAAGAGGACT	TGTGCAAACA	CTTCCTCTCT	GGACAAGGAG
TGAGTCTGTC	AGCCGCCGGA	CTTCTCCTGA	ACACGTTTGT	GAAGGAGAGA	CCTGTTCCTC
2650	2660	2670	2680	2690	2700
GAATGCAGGA	GGCCACCGCC	TGCAGTACAT	CTTGGAGTGT	TGGAGGGATG	TGCCTGCACT
CTTACGTCCT	CCGGTGGCGG	ACGTCATGTA	GAACCTCACA	ACCTCCCTAC	ACGGACGTGA

Corresponds to translational start site in rat/human GLP-2R gene.

2710	2720	2730	2740	2750	2760
TGTGAAAGGG	CGCCAGAAGG	ACGAGGCCCC	AACCAAGCCC	GGCAGTGCCC	AGTAGATGCA
ACACTTTCCC	GCGGTCTTCC	TGCTCCGGGG	TTGGTTCGGG	CCGTCACGGG	TCATCTACGT
2770	2780	2790	2800	2810	2820
GAGAGCGTCC	CTGCCCCGGG	CGCACAGTWG	GGCTCCCTGC	GGCCCAGGGG	CCTGAGTCTC
CTCTCGCAGG	GACGGGGCCC	GCGTGTCAWC	CCGAGGGACG	CCGGGTCCCC	GGACTCAGAG

FIG. 1c

Putative translational start site in murine GLP-2 Receptor gene.

2830	2840	2850	2860	2870	2880
TCCACKCCCA	CGGGATGCGT	CGGCTCTGGG	GCCCTGGGAC	GCCCTTCCTC	TCCCTGCTTC
AGGTGMGGGT	GCCCTACGCA	GCCGAGACCC	CGGGACCCTG	CGGGAAGGAG	AGGGACGAAG
2890	2900	2910	2920	2930	2940
TGCTGGTTTC	CATCAAGCAA	GTAAGAACAG	ATTTTTATTC	CTCATTCGTC	TTGTTAATAT
ACGACCAAAG	GTAGTTCGTT	CATTCTTGTC	TAAAAATAAG	GAGTAAGCAG	AACAATTATA
2950	2960	2970	2980	2990	3000
TATCAGTTGT	GCATGTTTTC	TGAGTGTACA	AGCAATTTAG	GCCCCGTGTA	GGCAATTTGG
ATAGTCAACA	CGTACAAAAG	ACTCACATCT	TCGTTAAATC	CGGGGCACAT	CCGTTAAACC
3010	3020	3030	3040	3050	3060
GTAAGAATAA	AACCATATTA	AGAAAATGAG	GCTCAACCAC	AACCCCAGTA	GCATTCTGCT
CATTCTTATT	TTGGTATAAT	TCTTTTACTC	CGAGTTGGTG	TTGGGGTCAT	CGTAAGACGA
3070	3080	3090	3100	3110	3120
CACTGTTCAT	ATTTTGGCTG	ATTTTTAAAA	AAATTCTCTT	TTCTGTGCAT	TATTTTACAC
GTGACAAGTA	TAAAACCGAC	TAAAAATTTT	TTTAAGAGAA	AAGACACGTA	ATAAAATGTG
3130	3140	3150	3160	3170	3180
AGCCGAAATT	....	....	....	....	....
TCGGCTTTAA	....	....	....	....	....

3'-End of murine GLP-2 Receptor gene sequenced to date.

FIG. 2

Sequence alignment of the 5' end of the mGLP-2 receptor gene with the 5' end of the cDNA encoding the rat GLP-2R.

Putative transcriptional start site.

5'-UTR nearly identical between rat and murine sequences encoding 5' end of GLP-2R.

```
                           10          20          30          40          50
MOUSE GLP-2R       1  AACACTTCCT  CTCTGGACAA  GGAGGAATGC  AGGAGGCCAC  CGCCTGCAGT
RAT GLP-2R         1  AACACTTCCT  CTCTGGACAA  GGAGGAGTGC  AGGAGGCCAC  CGCCTGCAGT

                           60          70          80          90         100
MOUSE GLP-2R      51  ACATCTTGGA  GTGTTGGAGG  GATGTGCCTG  CACTTGTGAA  AGGGCCCCAG
RAT GLP-2R        51  ACATCTTGGA  GTGTTGGAGG  GATGTGCCTG  CACTTGTGAA  CGGGCGCCAG

                          110         120         130         140         150
MOUSE GLP-2R     101  AAGGACGAGG  CCCCAACCAA  GCCCGGCAGT  GCCCAGTAGA  TGCAGAGAGC
RAT GLP-2R       101  GAGAATGAGG  CCCCAACCAA  GCCCGGCAGT  GCCCAGTAGA  TGCAGAGAGG

                          160         170         180         190         200
MOUSE GLP-2R     151  GTCCC-TGCC  CCG----GGC  GCACA----G  TWGGGCTCCC  TGCGGCCCAG
RAT GLP-2R       151  CACCCGTGCC  CCGAGTGAGG  GCACAGCCAG  TGGGCATCCC  TGAGGCCCAG

                          210         220         230         240         250
MOUSE GLP-2R     201  GGGCCTGAGT  CTCTCCACKC  CCACGGGATG  CGTCGGCTCT  GGGGCCCTGG
RAT GLP-2R       201  GGGCCCGTTC  CTCTCCACTC  CCAACAGATG  CGTCTGCTGT  GGGGCCCTGG

                          260         270         280         290         300
MOUSE GLP-2R     251  GACGCCCTTC  CTCTCCCTGC  TTCTGCTGGT  TTCCATCAAG  CAAGTAAGAA
RAT GLP-2R       251  GAGGCCCTTC  CTCGCCCTGC  TTCTGCTGGT  TTCCATCAAG  CAAGTTACAG

                          310         320         330         340         350
MOUSE GLP-2R     301  CAGATTTTTA  TTCCTCATTC  GTCTTGTTAA  TATTATCAGT  TGTGCATGTT
RAT GLP-2R       301  GATCGCTCCT  CAAGGAGACA  ACTCAGAAGT  GCGCTAATTA  TAAGGAGAAG
```

Upstream Initiator ATG codon.

Downstream Initiator ATG codon.

Sequence alignment of the 5' end of the mGLP-2 receptor gene with the 5' end of the cDNA encoding the rat GLP-2R.

The 5' end of the cDNA encoding the rat GLP-2R (cloned by 5'-RACE) is presented in alignment with the corresponding region of sequence encoding the murine GLP-2R. The upstream initiator ATG codon is present in the rat sequence, and the downstream initiator ATG codon is conserved between in both the rat and murine sequences encoding the GLP-2R. The sequence corresponding to the putative 5'-UTR (untranslated region) is nearly identical between the rat and murine sequences presented.

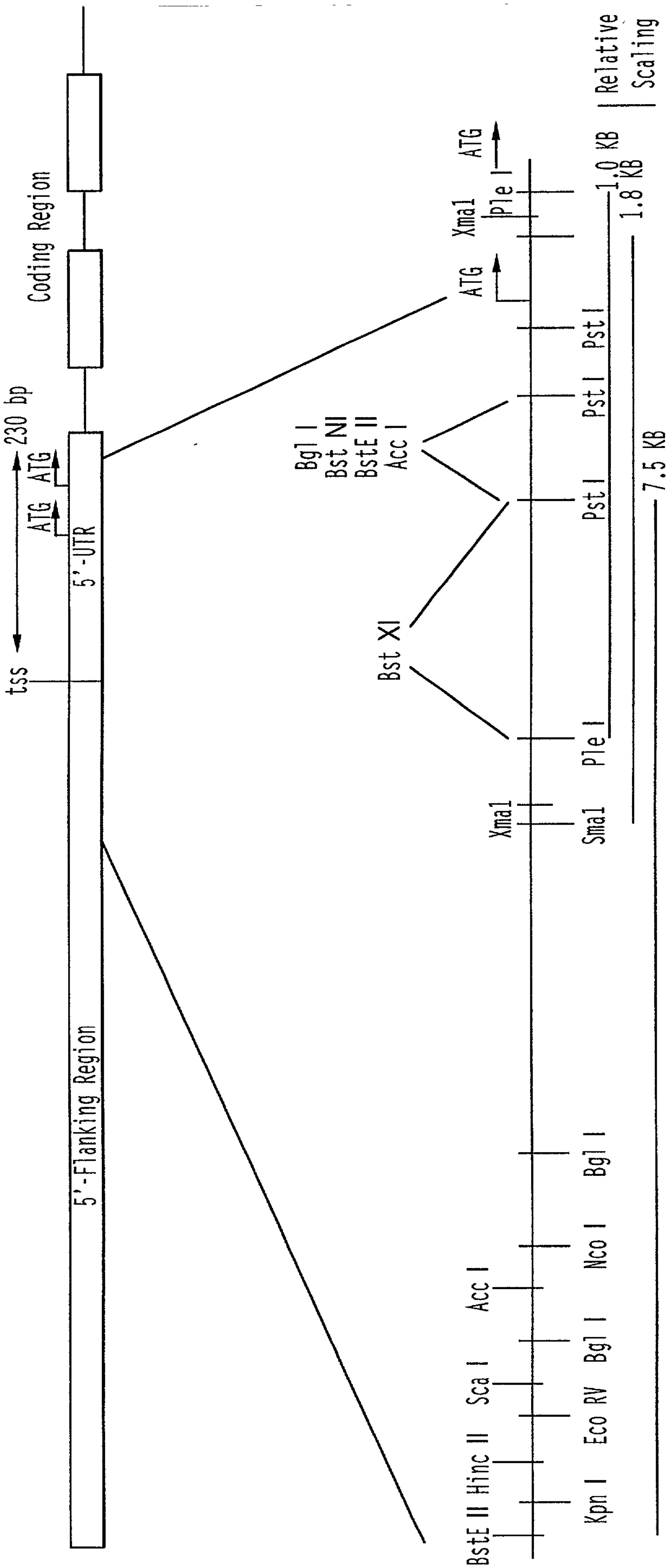
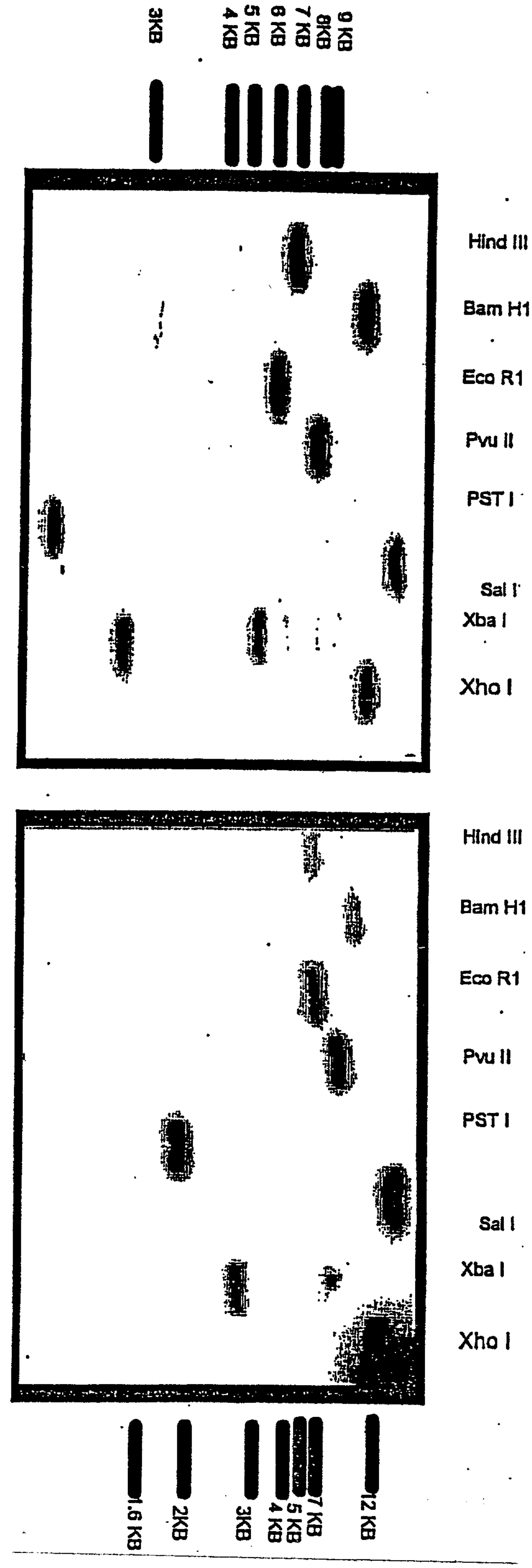

Coding Region
230 bp
ATG
ATG
tss
5'-UTR
5'-Flanking Region
Bgl I
Bst NI
BstE II
Acc I
Bst XI
ATG
Xma1
Ple I
ATG
Pst I
Pst I
Pst I
Ple I
Xma1
Sma1
BstE II
Hinc II
Sca I
Acc I
Kpn I
Eco RV
Bgl I
Nco I
Bgl I
1.0 KB
1.8 KB
7.5 KB
Relative Scaling

FIG. 3

FIG. 4


3KB
4 KB
5 KB
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7 KB
8KB
9 KB
Hind III
Bam H1
Eco R1
Pvu II
PST I
Sal I
Xba I
Xho I
Hind III
Bam H1
Eco R1
Pvu II
PST I
Sal I
Xba I
Xho I
1.6 KB
2KB
3KB
4 KB
5 KB
7 KB
12 KB

Title: GLP-2 RECEPTOR GENE
PROMOTER AND USES THEREOF
Inventor(s): Daniel J. DRUCKER
Appl. No.: 09/833,740

FIG. 5

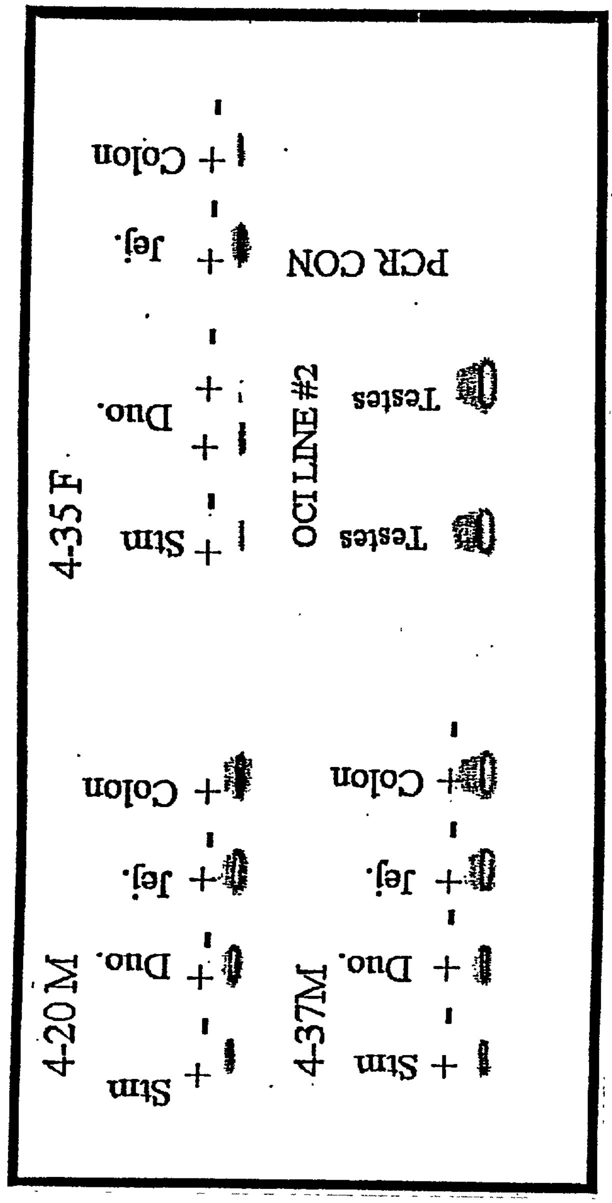

FIG. 6

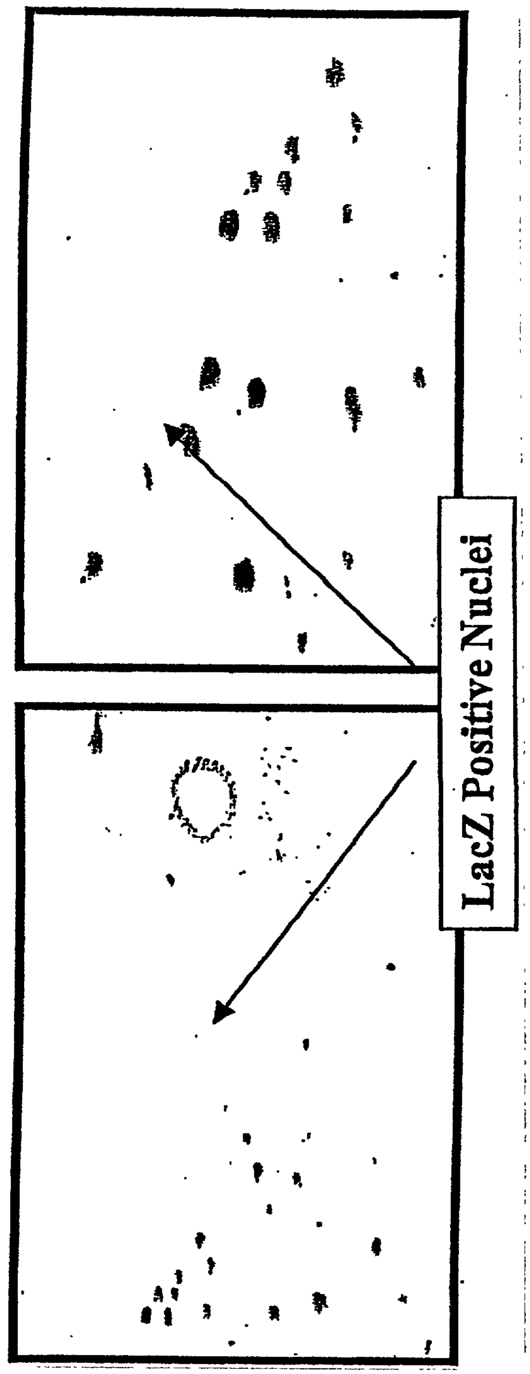

FIG. 7a

```
                  ↓ 5'-end                                                 5'-UTR
rat GLP-2R cDNA   aacacttcct ctctggacaa ggaggagtgc aggaggccac cgcctgcagt acatcttgga gtgttggagg gatgtgcctg cacttgtgaa cgggcgccag
                      M   R   P   Q   P   S   P   A   V   P   S   R   C   R   E   A   P   V   P   R   V   R   A   Q   P   V
rat GLP-2R cDNA   gaga ATG AGG CCC CAA CCA AGC CCG GCA GTG CCC AGT AGA TGC AGA GAG GCA CCC GTG CCC CGA GTG AGG GCA CAG CCA GTG
                   G   I   P   E   A   Q   G   P   V   P   L   H   S   Q   Q   M
rat GLP-2R cDNA   GGC ATC CCT GAG GCC GAG GGG CCC GTT CCT CTC CAC TCC CAA CAG ATG
```

FIG. 7c

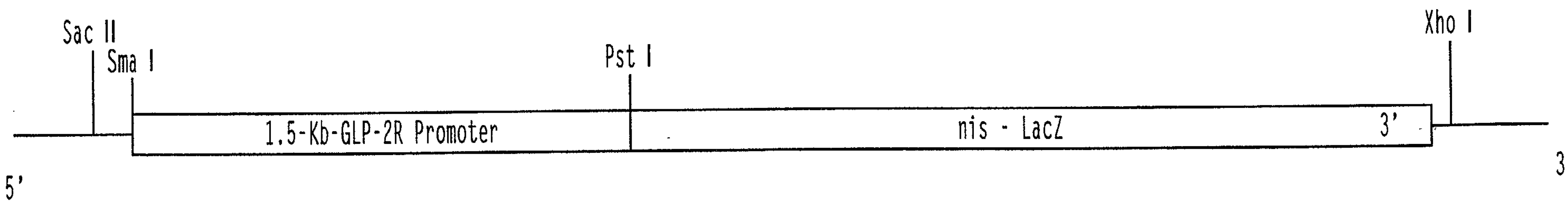

FIG. 7b

```
mouse GLP-2R    atgtcttgct ttttcttctg ggcttgctga ggaagtccca ggcagcgtag acgtcttggg ggtaggtctg ggaaaaatct
human GLP-2R    ccgccttgtt ctttctcctc agcctgtcaa ggaagtccca gaaagcacag ctgacttagg ga-aggtctg ggaaaaatct
            -203                                NF-Kappa B

mouse GLP-2R    cccaagattt aggaggggca --ggcggggg atgagaaact tggagattcg gtagatcgct gt---agagc aactcagaca
human GLP-2R    ccctgctttt gg-gggggca ggggcggggg atgagccagg gccgagaagg aactctgaag actccgtaga ttgctctaga
            -123                  Spl    Sp1  GATA-1            +1
rat GLP-2R                                                     aacactt cctctctgga caaggaggag tgcaggaggc
mouse GLP-2R    gtcggcggcc ---------- ------tgaa gaggacttgt gcaaacactt cctctctgga caaggaggaa tgcaggaggc
human GLP-2R    ccgcctcaga cactctcggc gcagcgtgga gaggatttgt gcaaacattt cctctgtgga ccaagaggaa tgcaagagga
            -43                                  CdxA
rat GLP-2R      caccgcc tgca  gtacatctt ggagtgttgg agggatgtgc ctgcacttgt gaacgggcgc caggaga ATG AGG CCC
mouse GLP-2R    caccgcc tgca  gtacatctt ggagtgttgg agggatgtgc ctgcacttgt gaaagggcgc cagaagg ACG AGG CCC
human GLP-2R    ggctgcc tgcg  gtgcatctt ggacggctag agagatgtac ccctacttgt gaaggtgcac gaggaag ATG AAG CTG
            38       Pst I
rat GLP-2R      CAA CCA AGC CCG GCA GTG CCC AGT AGA TGC AGA GAG GCA CCC GTG CCC CGA GTG AGG GCA CAG CCA
mouse GLP-2R    CAA CCA AGC CCG GCA GTG CCC AGT AGA TGC AGA GAG C-- --- --- -GT CCC TGC CCC GGG CGC ACA
human GLP-2R    GGA TCG AGC AGG GCA GGG CCT GGG AGA GGA AGC GCG GGA CTC CTG CCT GGC GTC CAC GAG CTG CCC
            114                                                       M   R   R   L   W   G
rat GLP-2R      GTG GGC ATC CCT GAG GCC CAG GGG CCC GTT CCT CTC CAC TCC CAA CAG ATG CGT CTG CTG TGG GGC
mouse GLP-2R    GTW GGG CTC CCT GCG GCC CAG GGG CCT GAG TCT CTC CAC KCC CAC GGG ATG CGT CGG CTC TGG GGC
human GLP-2R    ATG GGC ATC CCT GCC CCC TGG GGG ACC AGT CCT CTC TCC TTC CAC AGG AAG TGC TCT CTC TGG GCC
            180 P   G   T   P   F   L   S   L   L   L   V   S   I   K   Q
rat GLP-2R      GCT GGG AGG CCC TTC CTC GCC CTG CTT CTG CTG GTT TCC ATC AAG CAA
mouse GLP-2R    GCT GGG ACG CCC TTC CTC TCC CTC CTT CTG CTG GTT TCC ATC AAG CAA gtaagaacag---- --atttttat tcctcattc
human GLP-2R    GCT GGG AGG CCC TTC CTC ACT CTG GTC CTG CTG GTT TCC ATC AAG CAA gtaagagcagttca ttattattat tattatcag
            246
```

Title: GLP-2 RECEPTOR GENE
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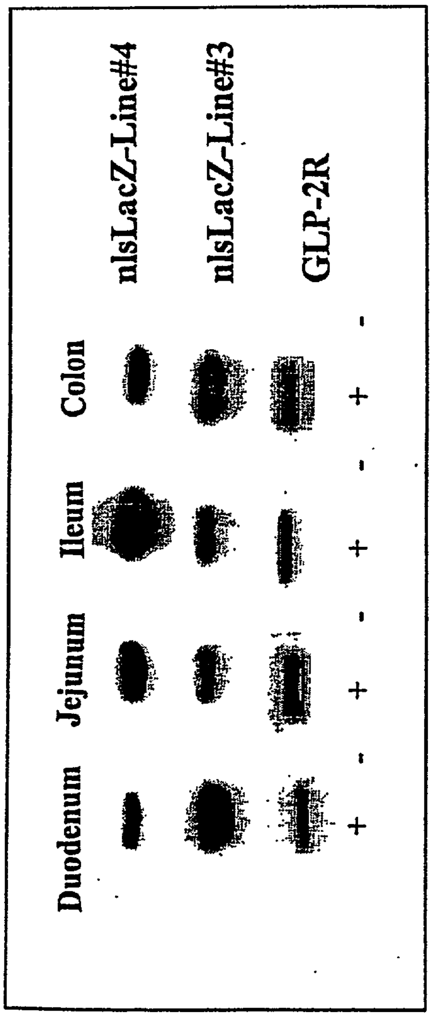


FIG. 8a

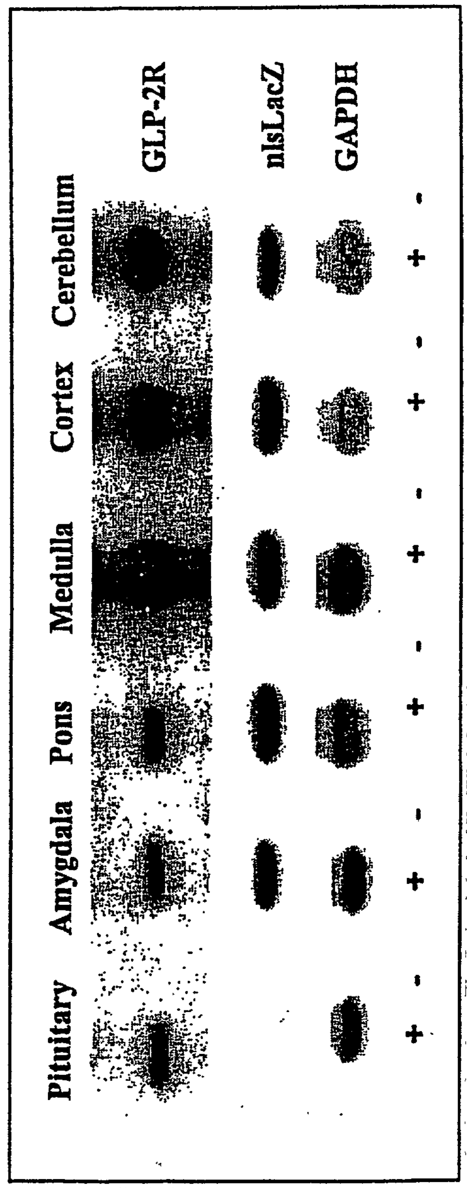


FIG. 8b

Title: GLP-2 RECEPTOR GENE PROMOTER AND USES THEREOF
Inventor(s): Daniel J. DRUCKER
Appl. No.: 09/833,740

FIG. 8c

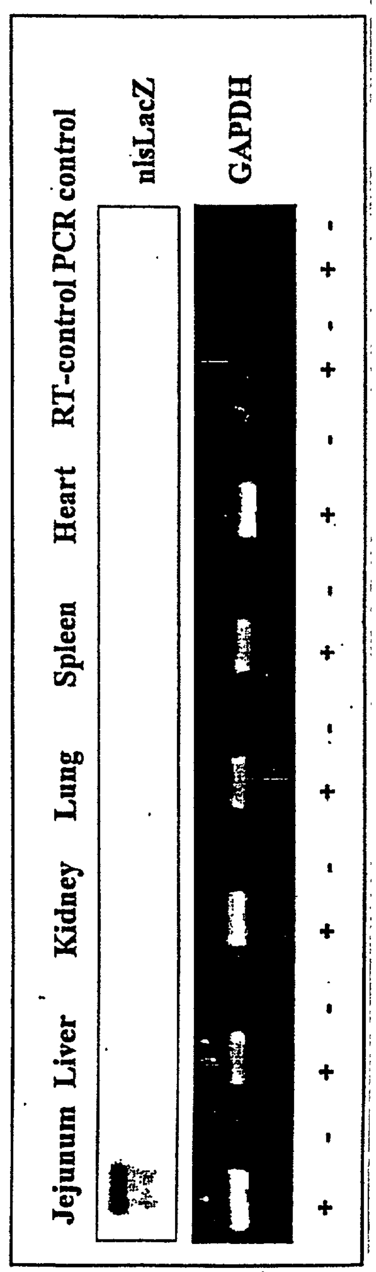


FIG. 8d

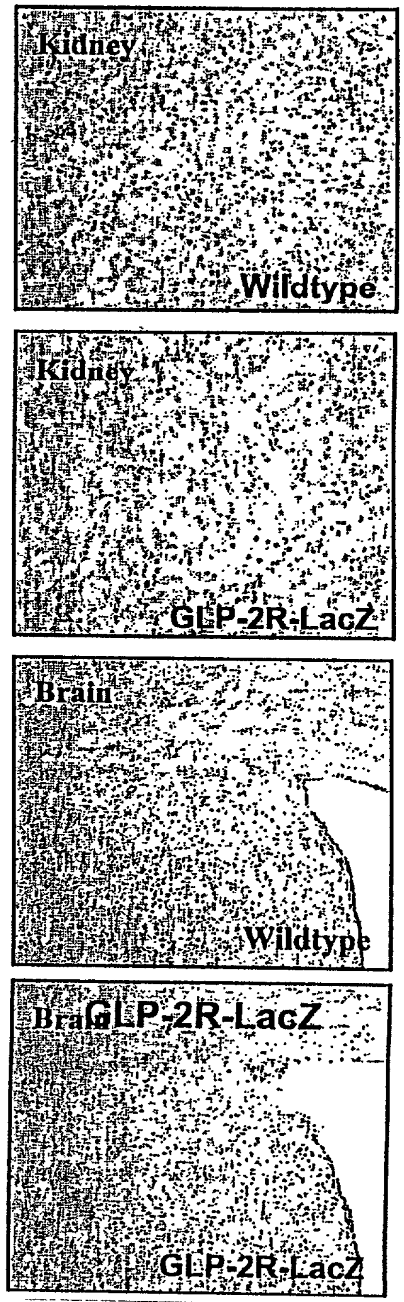
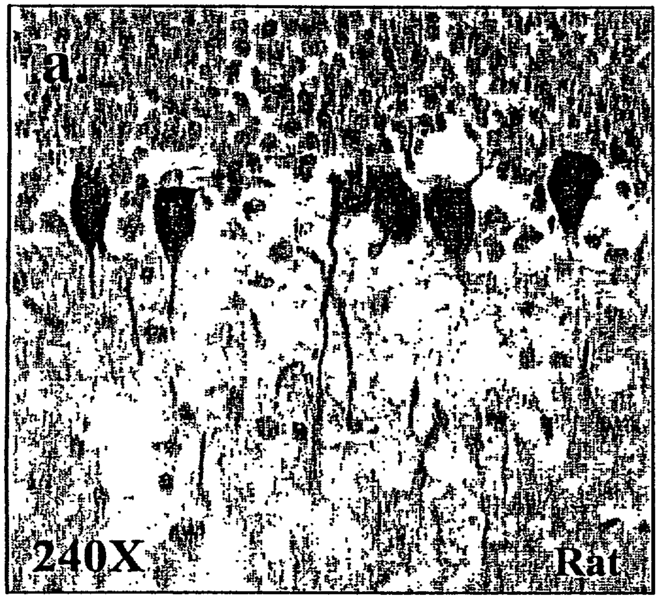

Kidney
Wildtype
Kidney
GLP-2R-LacZ
Brain
Wildtype
Brain
GLP-2R-LacZ
GLP-2R-LacZ

FIG. 9a

GLP-2R



Preimmune

FIG. 9b

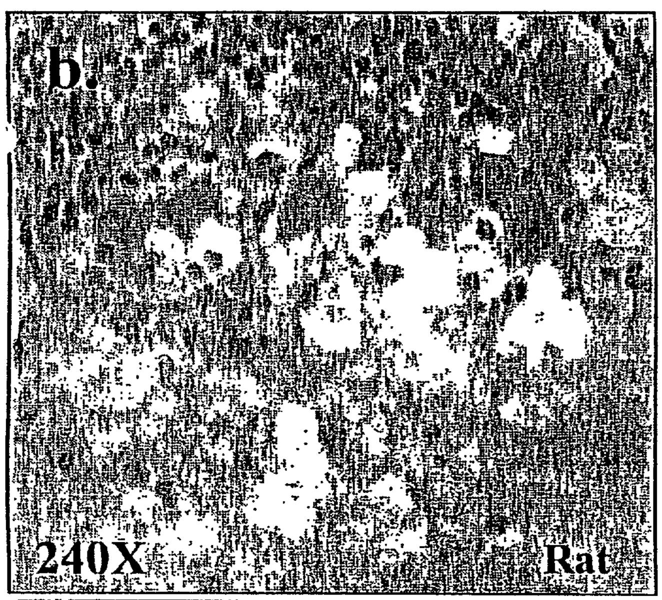


FIG. 9c

GLP-2R

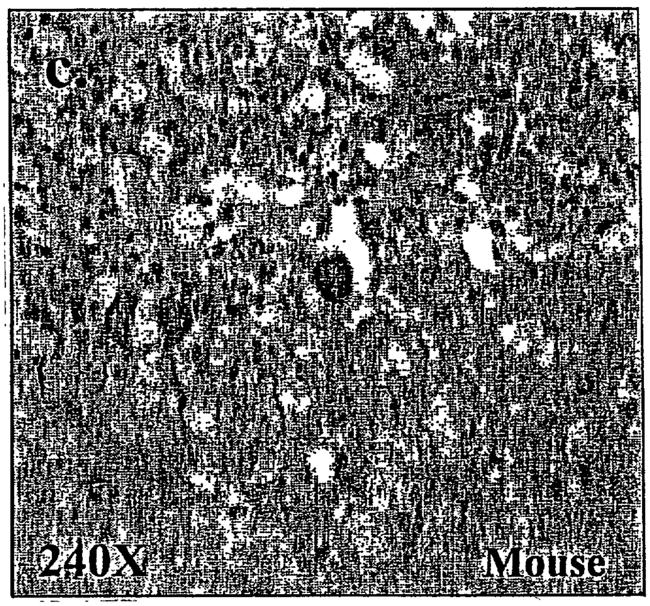


FIG. 9d

Preimmune

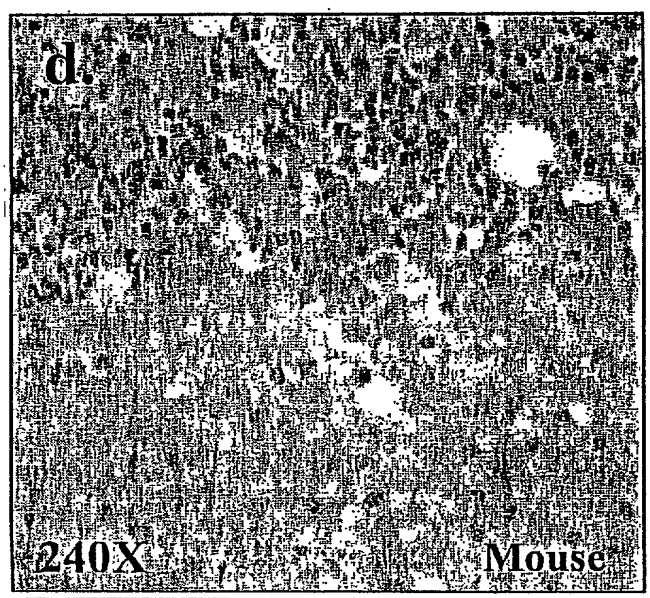


FIG. 9e

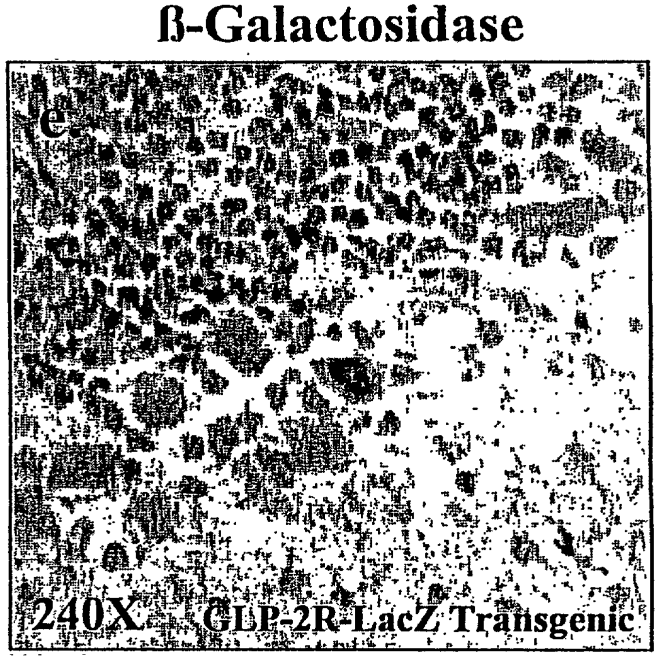
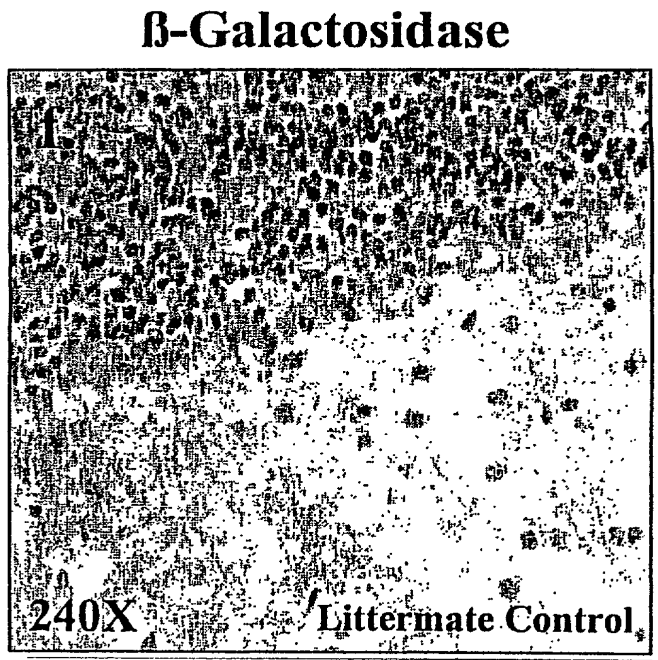

ß-Galactosidase
e
240X
GLP-2R-LacZ Transgenic

FIG. 9f


ß-Galactosidase
f
240X
Littermate Control

GLP-2R

FIG. 10a

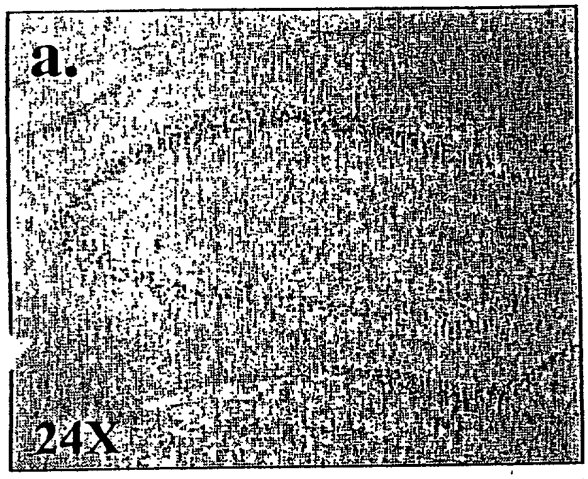
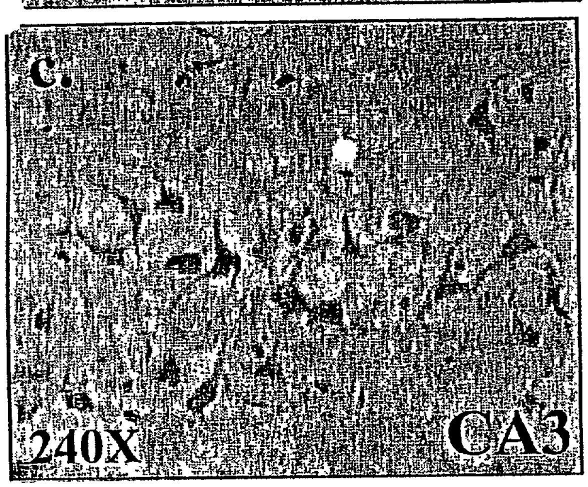


FIG. 10b

FIG. 10c



β-Galactosidase

FIG. 10d

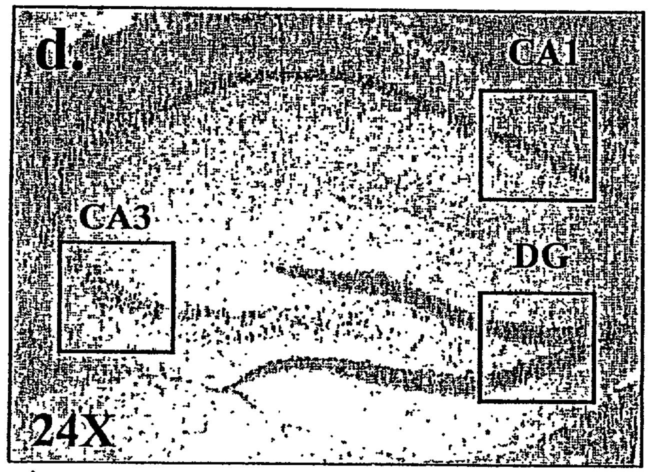


FIG. 10e

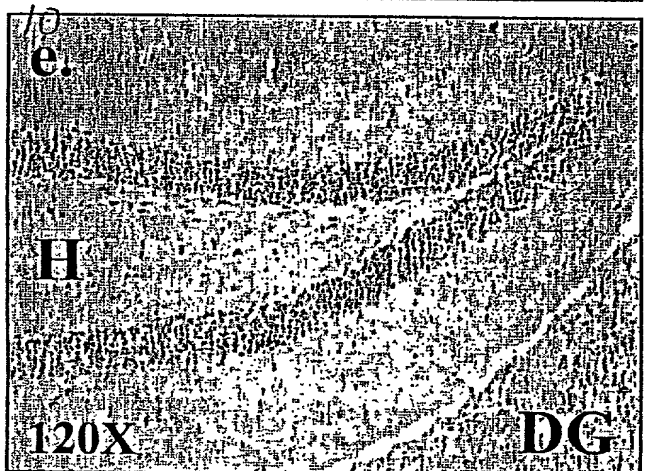
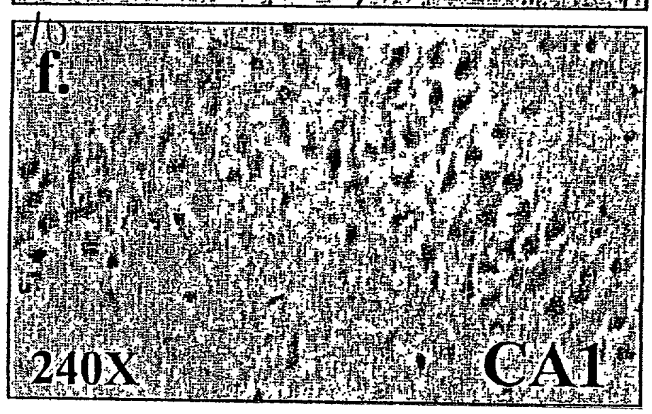


FIG. 10f



β-Galactosidase

FIG. 10g

FIG. 10h

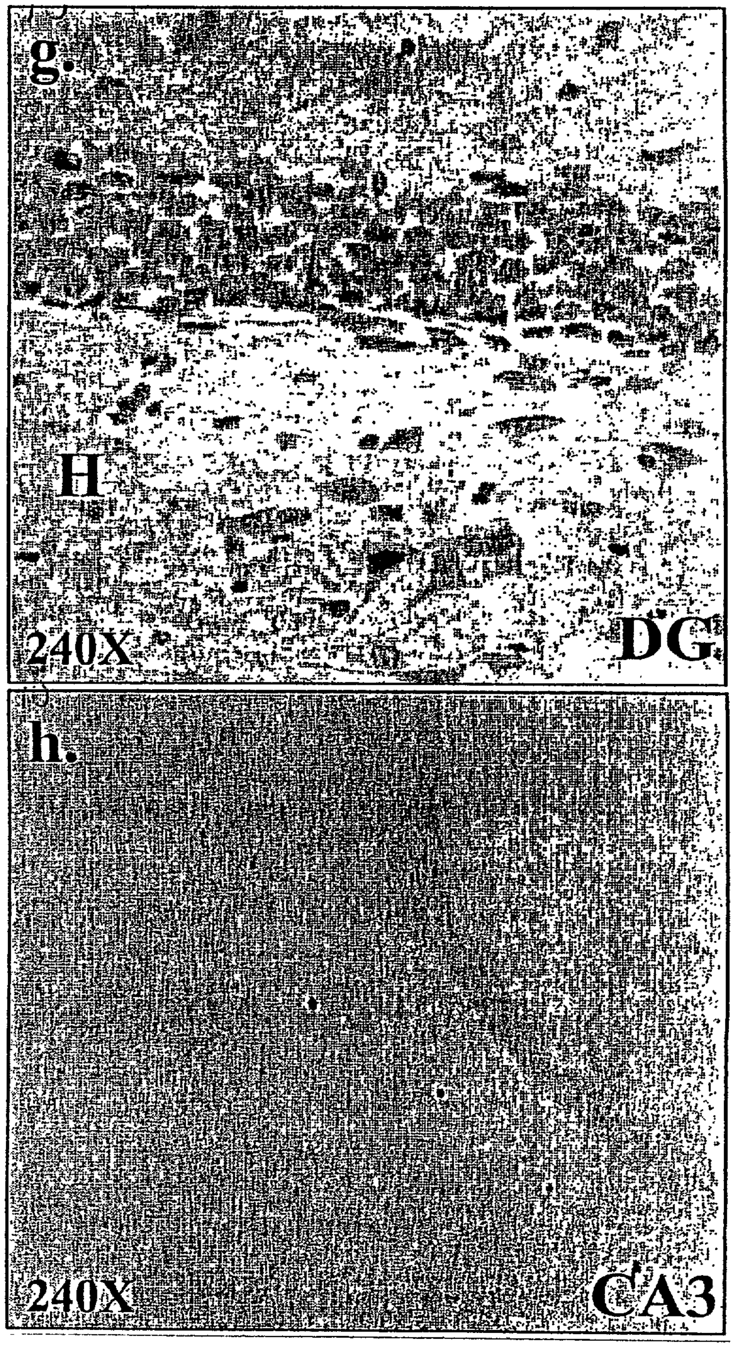


FIG. 11a

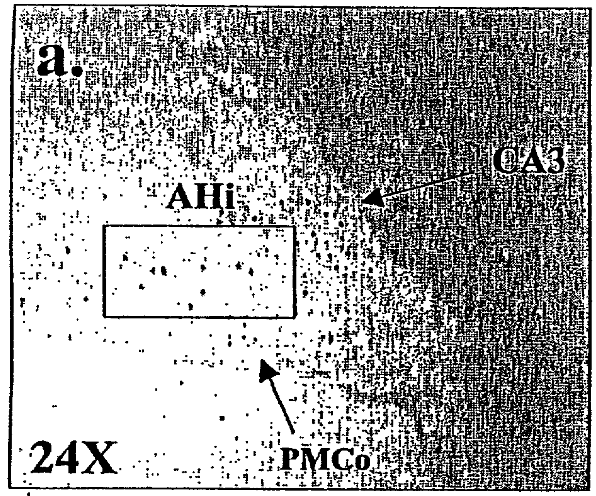


FIG. 11b

FIG. 11c

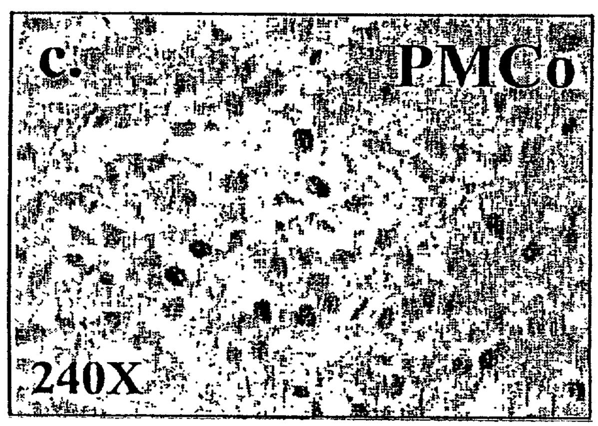


FIG. 11d

FIG. 11e

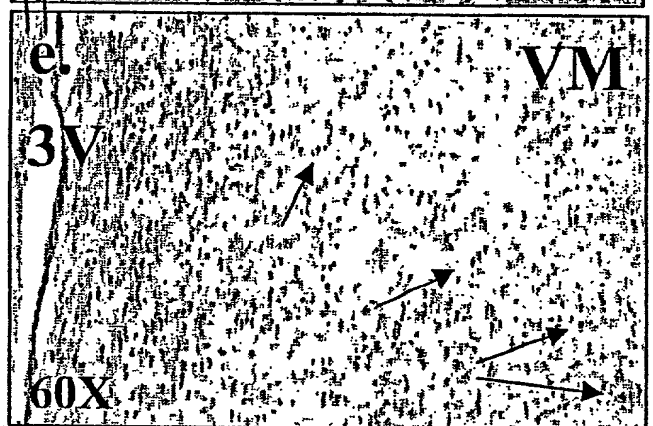


FIG. 11f

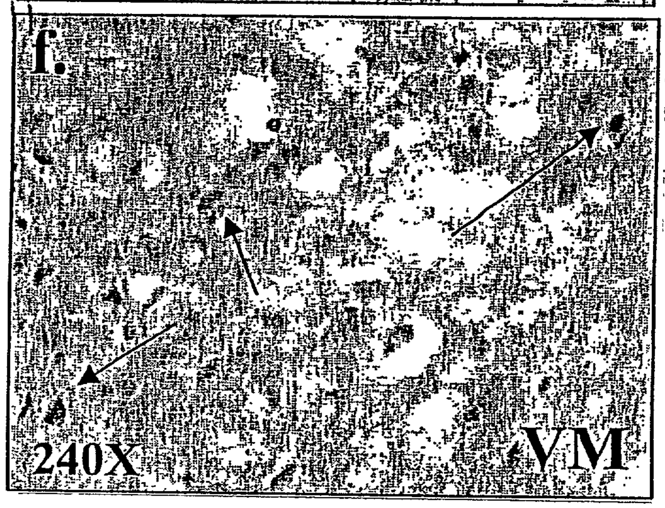


FIG. 11g

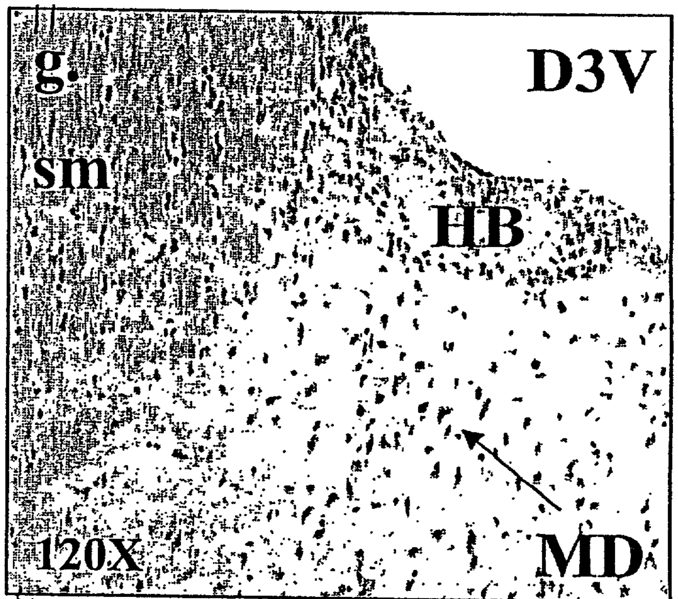


FIG. 11h

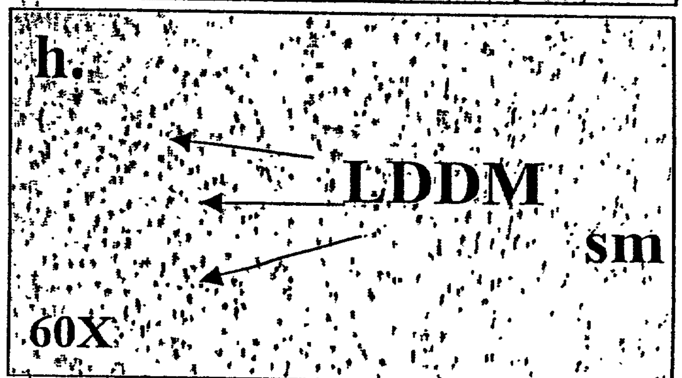


FIG. 11i